T Y P H U S G R O U P O F F E V E R S

with Special Reference to the Type of Fever found in KENYA.

by

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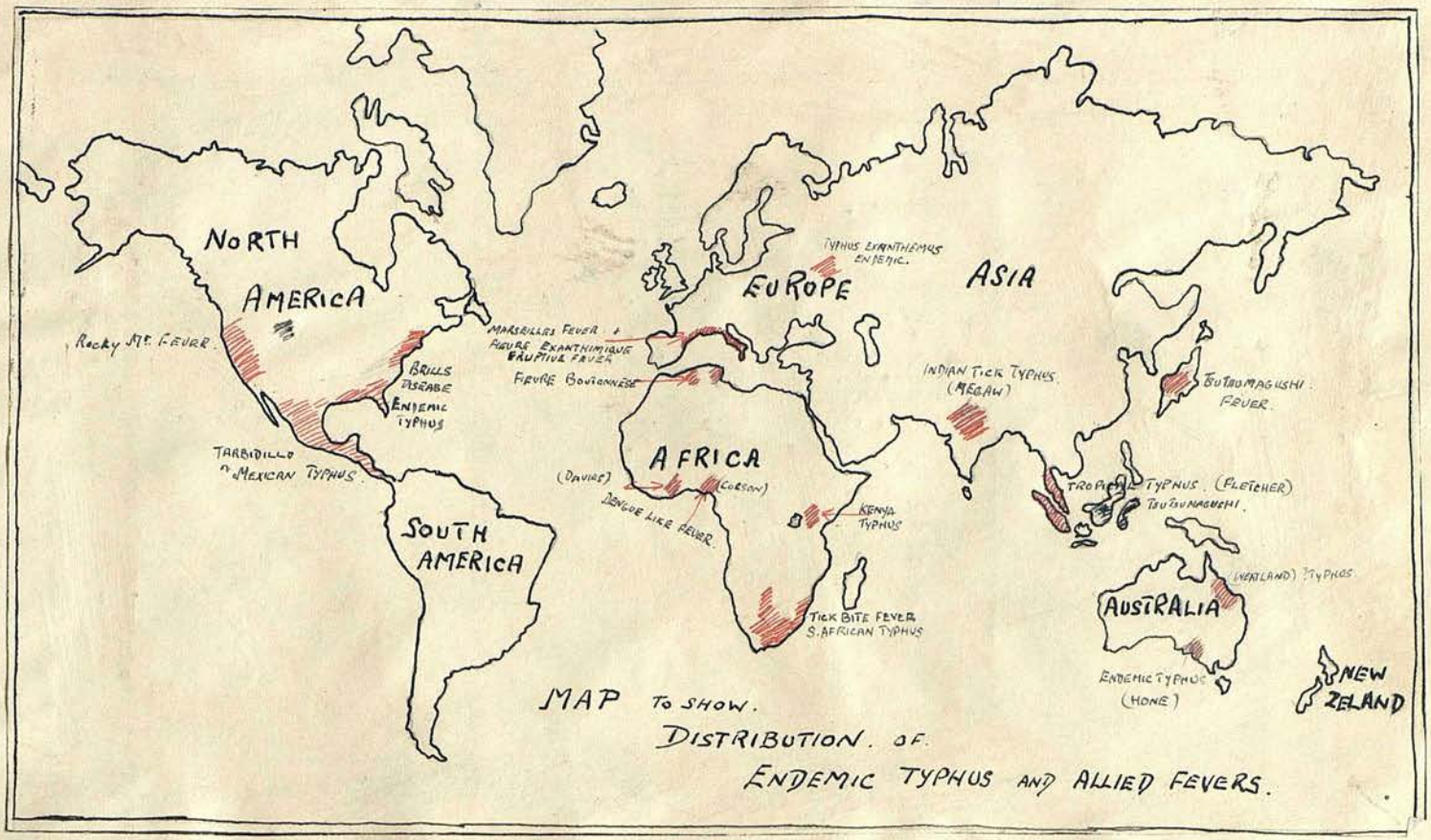


MAP TO SHOW.
DISTRIBUTION. OF.
ENDEMIC TYPHUS AND ALLIED FEVERS.

INTRODUCTION.

During the last ten or fifteen years there has been considerable interest aroused by the publications from all over the world (see map) of fevers that resemble Typhus Exanthemus clinically, but which appear to differ in certain respects in their etiology.

The fevers that have been described by the various authors are endemic in their respective countries, cases occurring sporadically each year.

There does not appear to be any person to person infection in these fevers and this has led to their being differentiated from Typhus Exanthemus which is known to occur in epidemics and has been called an infectious disease.

It is known that Typhus Exanthemus can be prevented by the exclusion of lice or its excreta from contact with the individual and so the disease is not strictly speaking infectious, but contagious, infection being passed by means of the louse. In the majority of the fevers that have been described, the carrying agent is thought to be some insect other than the louse. The insects that are suspected are ones that do not habitually live on man but only bite them occasionally, hence the unlikelihood of person to person infectivity in these fevers.

The fevers have been given numerous different names, each country and author giving its or his own name for their own special fever, and so there has arisen a great deal of confusion with regard to these fevers.

It is the purpose of this thesis firstly, to describe in detail the disease as it is found in Kenya and the results of investigations into its etiology that have been carried out recently, secondly, to give a brief description of the other fevers that occur elsewhere in the world and, thirdly, to endeavour to correlate the various fevers and bring them together into one group and to show that all these fevers are varieties of Typhus Exanthemus.

THE DISEASE IN KENYA.

History.

In 1920 Gilks[1] first described a few cases occurring in the European Hospital. One death occurred amongst his series and this induced him to publish his records to stimulate further investigation.

Clearkin[2] in the following year reported a few cases, some of which showed a positive Weil Felix Reaction, definitely establishing the disease as belonging to the Typhus group of fevers.

In 1925 Anderson[3] published the first important clinical description of the disease as it occurs in Kenya.

DISTRIBUTION IN NAIROBI.

DISTRICT	NUMBER OF CASES
1. Kilimani (inc. Upper Hill Estate)	14
2. Hill District	8
3. Commercial Area	2
4. Parklands (Lower)	2
5. Parklands (Upper)	1
6. Muthaiga	4

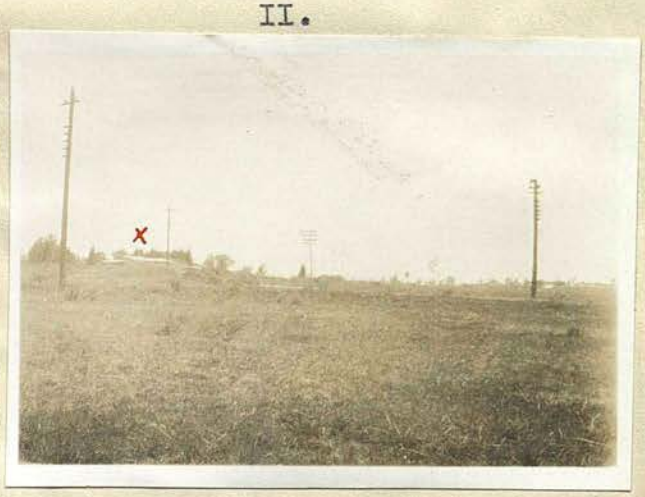
Total No. of Cases 31.

Percentage of Cases Occurring in First Two Districts 71%.

PHOTOGRAPHS KILIMANI DISTRICT.

I

II.



III.

IV.

Case occurred in house here.

From Main Road looking over to Kilimani.

Fig.V.

In 1930 Cormack and Jewell[4] described the disease in greater detail in comparing it to other types of the Typhus group.

Distribution.

The disease is endemic in the highlands of Kenya, a few cases occurring sporadically each year.

The majority of the cases recorded in this article have occurred in Nairobi or its suburbs.

Cases have been reported from Nyeri and Nanyuki Districts by Doig and from Nakuru District by Henderson.

A very few cases have been reported this year from Mombasa, which is at sea level.

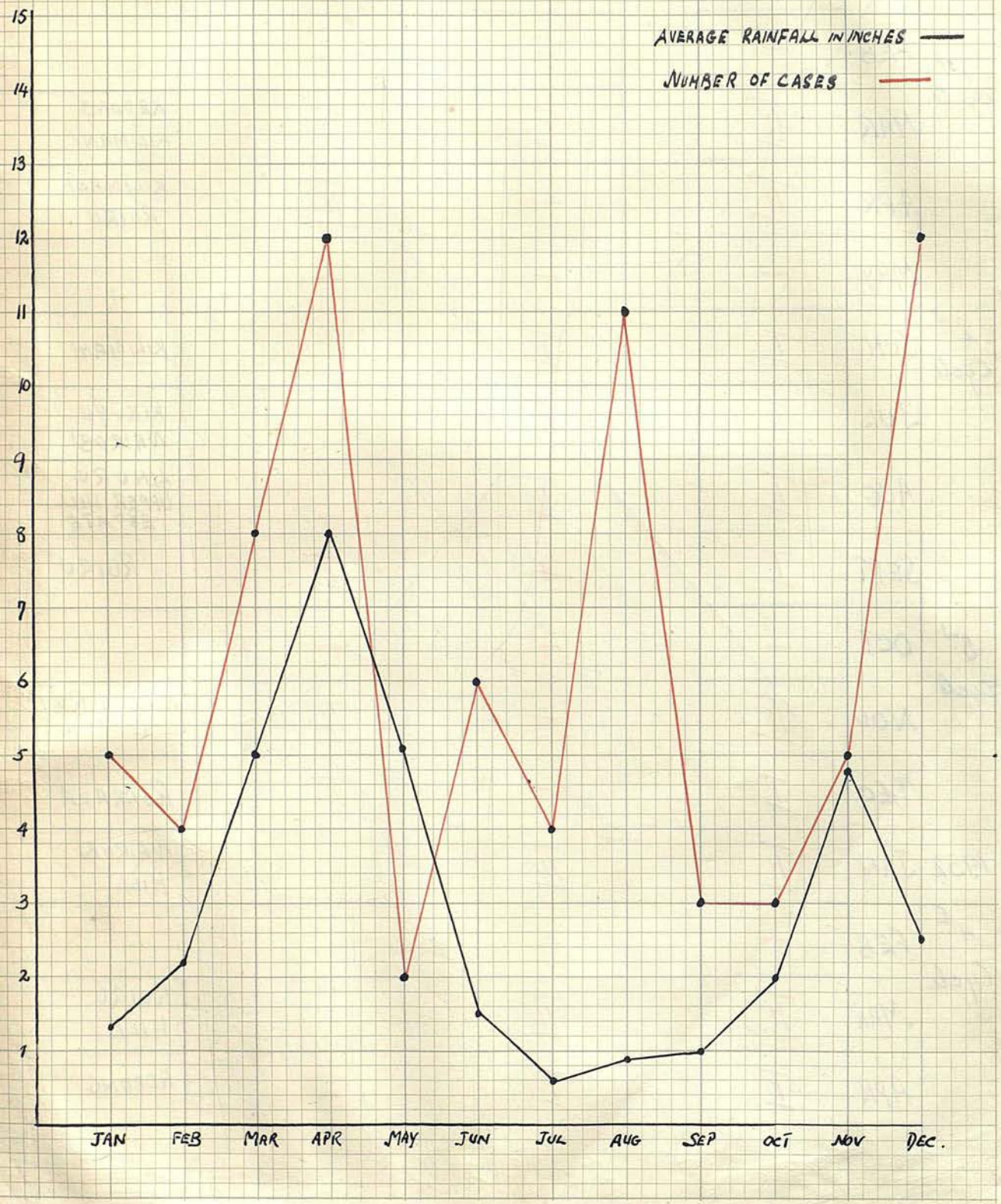
I have also had cases from farms between Nairobi and Ruira and on the Aberdain Mountains.

Now as regards the cases in Nairobi and district, it is interesting to note that the majority of them have occurred in a district of Nairobi known as Kilimani and its neighbouring districts known as Upper Hill Estate and the Hill. (see Table I)

This area lies on higher ground than the town itself and is not a very thickly populated area. It is a grassy plateau, and a great many houses abut onto this uncultivated land. This area is in complete contrast to a thickly populated area known

Fig II.

TABLE COMPARING AVERAGE RAINFALL IN NAIROBI WITH NUMBER OF CASES 1920 - 1931



as Lower Parklands, where there is a house on almost every half-acre of land and almost no waste land. Very few cases have occurred in Parklands within recent years.

It would appear, therefore, that there is some important etiological factor to be found in the Kilimani area. The grassy wasteland is possibly the deciding factor and this raises the question of rodents and their fauna, which abound in the long grass, as being the carrying agents of the disease in Kenya.

Seasonal Incidence.

Jewell and Cormack reported that "the disease although spread over the whole year was more common from August to December," their figures being eleven to ten for the other months.

A study of the accompanying graph is of some interest. (Fig.II) The graph represents a comparison between the average rainfall in Nairobi over a period of twenty-one years and the number of cases over a period of eleven years.

My figures of recorded cases have been obtained from:

i. cases recorded by Gilks, Clearkin and Anderson,

ii. cases occurring in the European Hospital during 1930 and 1931,

iii. other cases notified from 1924 - 1929 and obtained from the M.O.H. of Nairobi.

iv. cases occurring in my own practice in 1930 and 1931.

It will be seen that cases have occurred in every month of the year, but there are three months - i.e. April, August and December - when the disease is more prevalent. It will also be noticed that these months are equidistant from each other. In other words there appears to be a four-monthly cycle. The first and the last waves occur at or about the rainy season. The middle wave (August) has a very small rainfall.

Now here we have a wave of the disease occurring three times a year; two peaks occur at or about the rainy season and the other during the dry season, which incidentally is also the cold season.

It would seem necessary to analyse the cases more fully.

The only difference I could find between my cases was the presence or absence of the initial bite or eschar, and with this in view I have made a table of my cases over the year 1931, dividing the year into three periods - January to April, May to August, and September to December - and noting the presence or absence of the initial bite. (Fig.III)

		Nr of cases	Tache noire	No tache noire	Place
1931 1st cycle	JAN	I	–	I	RUARAKA
	FEB	–	–	–	
	MAR	II	I	I	KEDONG KILIMANI
	APR	II	–	II	KILIMANI RUIRU
2nd cycle	MAY	–	–	–	
	JUN	I	I		KILIMANI
	JUL	II	II		KIKUYU NAIROBI
	AUG	II	II		LIMURU UPPER HILL ESTATE
3rd cycle	SEP	I	–	I	RUIRU
	OCT	–	–	–	
	NOV	II	–	II	KIKUYU RD " "
	DEC	I	–	I	RUARAKA
1932 4th cycle	JAN	II	II	–	NAIROBI HILL
	FEB	–	–	–	
	MAR	II	II	–	RUIRU HILL
	APR	I	I	–	KEDONG

As will be seen from the accompanying table, in which the first cycle in 1932 is included, it appears that the initial bite is present in all cases in the second and fourth cycle and is absent, except in one case, in the first and third cycle; that is to say the types of cases alternate. This may point to there being two or more vectors in this disease and the periodicity being in the nature of the vectors' life cycle or to certain climatic influences, different vectors being more abundant at certain times of the year.

This investigation would require to be prolonged over a number of years before a definite significance could be attached to any findings.

Doig of Nyeri tells me that the great majority of his cases occur during the long rains, i.e. in April, and out of his eighteen cases he has only seen two with the initial bite. On the other hand, the majority of Henderson's cases have occurred during the dry season and they have all had initial bites.

Age, Sex and Race Incidence.

The disease attacks either sex and at any age. The youngest of my series was 18 months and the eldest 54 years, but the disease is most common between 20 and 40 years of age.

Out of 79 cases of which I have records 46 were males and 33 were females, which is approximately the ratio between the European male and female population. All the cases in my series have occurred amongst the European population.

One case, a Seychellois, has been reported amongst the Asiatics and only two have been reported amongst the natives. The reason for this is probably on account of the rash being difficult to discern on the dark skin and that in all probability they are attacked when young and have raised an immunity against this disease in the same way that the population of Warsaw have raised an immunity against Typhus Exanthemus.

Incubation Period

This is difficult to elicit except in those cases with the initial bite or eschar. In these cases it appears to be anything from two to fourteen days.

In one of my cases the patient was bitten by a "fly" and developed symptoms eight days later. In another case the patient noticed a bite which was painful four days prior to rise of temperature. In another, a child was bitten by a tick which was picked off by its mother, the symptoms developing fourteen days later. Yet another patient was

bitten by "a minute black insect" below the right clavicle, developing her symptoms with a rigor two days later. These four cases all developed the typical eschar, or as the French so aptly term it, a 'tache noire' at the site of the bite.

The incubation period was eight days after the initial passage of the disease to a guinea-pig, but after subsequent passage from guinea-pig to guinea-pig it was lowered to five days.

Henderson tells me the incubation period has been eight to ten days in his cases.

Symptoms and Signs

Mode of Onset.

A few patients complain of slight malaise for a day prior to onset, which is usually abrupt.

In the first 24 hours the temperature rises to 102° or 103°, frequently with a rigor, accompanied by intense headache and pain in the back and limbs. The patient complains of intense headache on any ocular movement and there is often photophobia. The conjunctivae are suffused and the face is flushed, resembling the facies of measles. Insomnia is usually marked and nightmares are frequent. The patient has no inclination for food, occasionally there is vomiting, and constipation is usually present.

The Rash.

During the next few days the patient remains in the same state, headache and insomnia being the chief features. The temperature remains elevated with small daily remissions, rarely going below 101°.

Rash

On or about the 5th day the patient develops a rash, which is sometimes heralded by a rigor. There is often a generalised erythema from the beginning, which fades when the true rash develops.

The rash, which may be maculopapular or papular, develops slowly, fresh spots appearing throughout the course of the disease until the temperature subsides. They begin to fade two or three days after their appearance so that at the end there is a mottling, some of the spots being bright pink and others brown, as they turn through varying shades of reddish pink to purple, then brown. They disappear on pressure at first, but later leave a brown staining.

The papules are discrete and vary in size from a pin's head to a large pea, the bigger ones when fully developed being easily palpable and often tender to the touch.

The rash may be situated all over the cutaneous surface of the body, limbs, back, chest and abdomen being the commonest sites. A constant and characteristic feature of the rash is the presence of one or two spots on the palms of the hands and

the soles of the feet. The face is very commonly affected.

The rash resembles closely that of secondary syphilis.

Haemorrhagic spots have been described by some observers.

The intensity of the rash may vary from being very profuse, with its usual wide distribution, to the presence of only a few scattered spots. This scarcity of rash I have found to be more common in those cases with the initial eschar.

The residual pigmentation remains for a considerable period after the temperature has subsided, being discernible, in some cases, four or five weeks later.

Course.

Coinciding with the appearance of the rash, joint pains develop. These may be very severe and affect two or three joints at the same time. There is usually a mild dilirium and the patient takes no interest in his surroundings, preferring solitude. In severe cases the patient may lapse into a typhoidal state.

Thefastigium is reached about the eighth day and temperature subsides by rapid lysis, the fever lasting from ten to fourteen days in all. As soon

as the temperature subsides the patient as a rule feels markedly better, the spots begin to fade and the headache and joint pains cease abruptly. Occasionally there is a relapse for a day or two.

The relief experienced by the patient after a severe case is most noticeable. Having lived for what appears to have been an ageless time in a fantastic world where he was tortured by a ceaseless headache, he returns to the world weak but smiling and expressing the fervent hope that he will never experience a similar nightmare again.

In the very few cases with fatal termination, the patient continued in a drowsy and delirious state after the temperature had subsided, going into coma and dying within a short time.

Special Features.

Headache is one of the most constant features of the disease and is present from the onset, usually lasting until the temperature becomes normal.

The pain is situated behind the eyes and is both frontal and occipital, and if the eyes or the head as a whole is moved shooting pains in the head are complained of.

The scalp is often tender to light touch and, as described by the patient himself, it feels as

though the scalp was being raised up off the bone; firm pressure with the hands relieves this tenderness.

Joint Pains are a fairly constant feature, the pains being situated in and around the joints. There are usually two or three joints affected at the same time, one more severely than the others.

The most common joints to be affected are the wrist, small joints of the hands, elbows, shoulders and knees, though any joint may be involved.

Swelling round the affected joint has been described but in my experience there is no swelling, redness or heat in the affected joints. These joint pains appear about the fifth day with the onset of the rash, and their severity appears to vary in direct ratio with the profuseness of the rash; they disappear when the temperature begins to subside.

Painful areas - this is another constant feature of the disease appearing about the same time as the joint pains.

The painful spots lie where a bone appears near the cutaneous surface; they are most common over the occiput and occasionally fronto-parietal suture.

One patient described the effect of pressure on the painful area on the occiput saying "it felt as

though her eye on the affected side was being pushed out from behind."

These painful areas have also occurred on the ulna near the elbow, near the internal epicondyle of the humerus and over the head of the fibula, in fact they occur where nerves are in close connection to bones, e.g. the greater occipital, the ulnar and the common peroneal nerves.

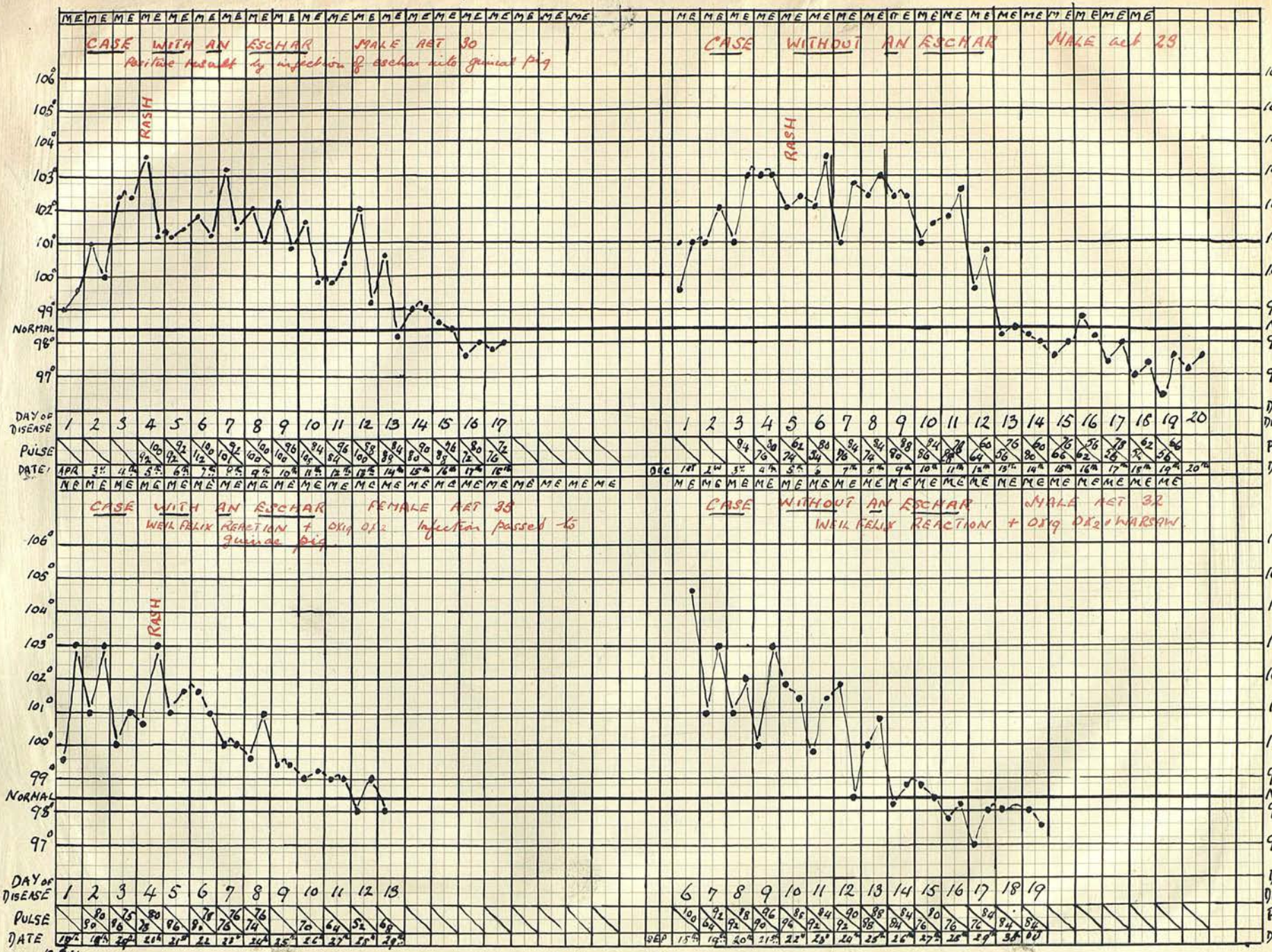
There is frequently a definite swelling in the region of these painful areas. In all probability these spots are in the nature of Typhus nodules.

Insomnia with mild delirium - this is always a marked feature. Patients when asked why they cannot sleep do not reply "because I have a headache," but say their brains are so active they are thinking and remain wide awake. They have a quiet delirium and are always conscious of their state, but can do nothing to rectify it.

Eyes. There is usually, in the early stages of the disease, marked photophobia, light increasing the headache. The conjunctivae are suffused but there is no actual conjunctivitis.

Tongue. The tongue in severe cases is invariably dry and covered with a thick brown fur. The dorsum is covered with a thick fur while the sides and tip

TEMPERATURE CHARTS



(Fig IV)

remain bright red.

Pulse - This is relatively slow in comparison with the height of the temperature except in the case of young children.

The accompanying temperature charts (Fig.IV) show that although the temperature is high, the pulse rate seldom rises above 100 per minute and is usually around 90 per minute.

The pulse is easily compressible and, in my experience, regular.

With the fall in temperature the pulse rate sometimes drops as low as 46 per minute.

Sore throat and cough. Sore throat is sometimes complained of and on examination the fauces are seen to be injected.

There is usually a short dry cough which appears to be due to an irritation of the larynx and trachea, which is possibly caused by the rash, as in all my cases the lungs have been normal.

Spleen. This is enlarged to percussion but is not always palpable. When palpable it is found to be soft and difficult to palpate, resembling the spleen found in typhoid.

Blood. Some observers state that there is a mild leucocytosis; in those cases in which I have done

FIG. V.

COMPARISON OF DIFFERENTIAL WHITE CELL COUNTS IN KENYA WITH THOSE IN SOUTH AFRICA.

CASE	POLYMORPHS	LYMPHOCYTES	EOSINOPHILS	LARGE MONONUCLEARS	INITIAL LESION	REMARKS.
1	69	24	1	6	–	
2	45	42	-	13	+	
3	48.3	48.3	-	3.4	+	THIS PATIENT HAD PHTHYSIS
4	60	15	-	25	–	
5	89	4	–	7	–	
6	82	12	–	6	+	
7	75	15	–	10	–	
8	72	27	–	1	+	
9	56	37	–	7	–	
10	65	25	–	12	–	
11	55	36	–	10	-	

Differential White Cell Counts in Kenya Cases.

CASE	NEUTROPHILS	EOSINOPHILES	BASOPHILS	LYMPHOCYTES	MONOCYTES	
1	63	–	–	33	4	
2	53	2	–	36	9	
3	66	–	–	28	6	
4	61	–	–	32	6	
5	72	–	–	27	1	
6	59	–	–	30	11	
7	61	–	–	35	4	
8	53	2	–	33	10	
9	55	–	1	37	7	
10	52	–	–	40	8	
11	70	2	–	23	5	
12	59	–	–	29	9	
13	54	–	–	40	6	
14	50	2	–	39	9	
15	52	1	–	41	4	
16	66	1	–	27	6	
17	56	–	–	37	5	
18	56	1	2	39	2	
19	48	–	–	50	2	
20	51	–	1	38	10	
TYPHUS	80	–	–	18	2	

White Cell Counts in Tick-bite Fever and Typhus in S.Africa (After Troup & Pijper).

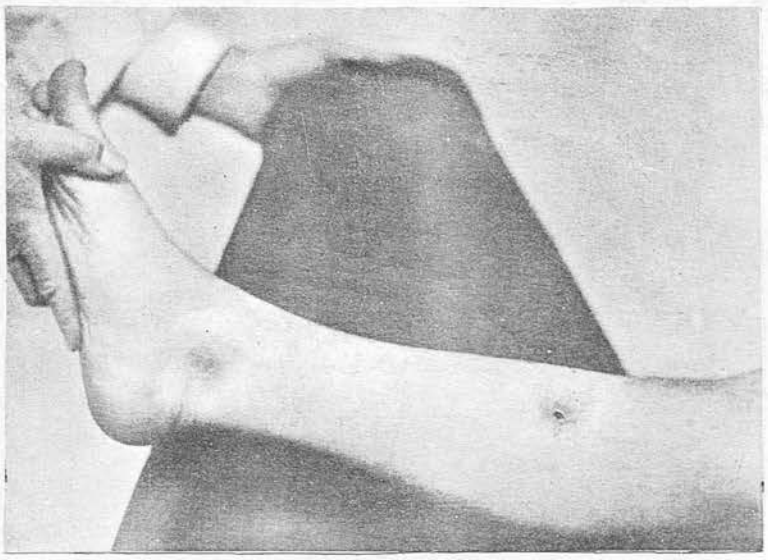
a white cell count I have not found any increase in the leucocytes, the count being within normal limits.

Anderson states that there is an increase in the number of red cells, a polycythemia. I have not verified this but I have had a case, however, in which the nose has bled on and off during the height of the fever, accompanied by a cyanosis.

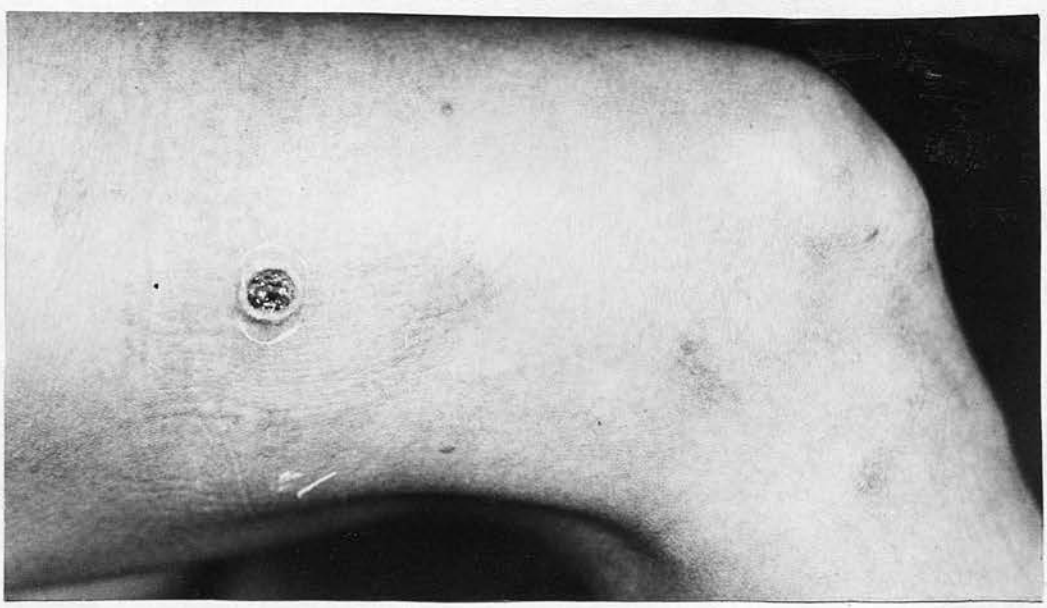
The differential white count appears to be within normal limits, some undoubtedly show a relative lympocytosis while others are normal. (figure 5)

There appears to be a definite though slight increase in the large mononuclear cells in the majority of cases.

Troupe and Pijper, in their paper on Tickbite Fever in South Africa,(5) endeavour to differentiate between typhus (those cases without an eschar) and "Tickbite Fever" (those with an eschar). Among other differences they show that whereas in typhus the count is normal (only one case shown) in "Tickbite Fever" there is a relative lymphocytosis. My cases do not show any uniformity in this direction, some cases with the initial eschar showing relative lympocytosis and others normal, and vice versa (see comparison of Troupe and Pijper table with Kenya cases: figure 5). It would appear that in this



Initial Bite in Second Stage
After Jewell & Cormack.



Initial Bite. Stage of Ulceration.

disease there is no constant deviation from the normal white cell count or differential count, except possibly in decrease of eosinophils.

Urine. The urine is febrile in type and there is often a slight trace of albumin in the early stages, but no evidence of nephritis. The urine has been sterile in all cases that it has been cultured, no B. Proteus having been grown.

Initial Bite, Eschar or Tache Noire. This has occurred in about 50% of the cases in which I have been able to obtain definite records, i.e. 34 out of 68: Nakuru district 17 out of 19, Nyeri district 2 out of 18 and Nairobi district 15 out of 31. The leg and thigh are the most common sites for the bite but it may be found anywhere.

The bite, which usually starts as a little pimple, is usually accounted for by the patient as the bite of an insect.

During the next few days considerable local reaction develops; when seen in this stage there is a small pustule with a red raised area of skin surrounding it between the size of a shilling and a half-crown piece.

The lymp glands draining this area become enlarged and tender.

The pustule dries up and becomes a bluish black

scab with a small ulcer in the centre, the rest of the spot remaining red and raised.

The scab drops off leaving an ulcer, and the local reaction subsides.

It takes in all about three weeks from the time the patient is bitten until the ulcer is healed.

Glandular Enlargement. In those cases only that have an initial bite is there a marked enlargement and inflammation of glands, and then only in those draining the area of the bite.

These glands are discrete, large and tender, and the skin over them is often inflamed but suppuration never occurs.

In most cases, irrespective of the bite, the small glands of the neck, notably the posterior group, become palpable; they are small, shotty and not tender to the touch. Sometimes other glands are palpable, especially the epitrochlear, but as insect bites of all sorts are so common in Kenya very little significance, if any, can be placed on the presence of palpable glands.

Blood Pressure is low. It is low early on in the disease and remains so for some considerable time, thus prolonging the convalescence.

The lowest I have recorded was systolic 88mm. with diastolic 64mm. In this case the systolic

pressure was 108mm. one month after the illness. In the highlands of Kenya the normal blood pressure tends to be at a lower level than at sea level so that in all probability 108mm. was the normal blood pressure in the above case, thus giving a drop of 20mm. during the fever.

Lowering of the blood pressure has not been noted by previous authors as occurring in Kenya typhus, but Gulmo[6] noted this phenomenon as occurring in his cases.

Other organs appear to be normal; some observers state that there is an increase in the reflexes but I have not found this is my series.

Diagnosis should be readily made even in the stage of invasion, as the disease can usually be diagnosed before the rash appears.

The combination of high temperature, slow pulse, intense headache and an angry-looking bite with enlarged and painful glands leads one to suspect this disease. The appearance of a rash on or about the fifth day confirms one's diagnosis.

When it comes to cases without an obvious bite, diagnosis is more difficult before the rash appears but the following signs and symptoms may help one to the correct diagnosis.

i. High temperature with only small daily remissions;

ii. Relatively slow pulse;

iii. Intense headache with insomnia;

iv. Suffused conjunctivae with photophobia;

v. Tongue with furred dorsum and bright red tip and sides.

Weil Felix Reaction,

A positive reaction confirms the diagnosis but it is seldom positive at the beginning of the disease and only becomes so towards the end or about the twelfth day, and during convalescence it is at its maximum. Therefore its practical value is considerably lessened as an aid to diagnosis and, more important still (as far as the general practitioner and patient's relatives are concerned) to prognosis, as by the twelfth day, in the majority of cases the patient is either recovering or is in extremis.

Unfortunately by no means every case in this country shows a positive Weil Felix reaction at any time in the course of the disease.

In my first few cases the reaction was not performed. However, in the case that Rickettsia-like bodies were identified in a guinea-pig affected by means of the intra-peritoneal injection of the eschar, the reaction was performed and was positive to a titre of 1/80 to B. Proteus OX_{19} and OX_2. Being elated by this fact my next two cases, almost identical with the positive one, also had

Weil Felix reactions done - both were negative to all available strains.

Since then I have had one more positive to OX_{19} and OX_2 in a case without an eschar.

DeSmidt of the Kenya Medical Research Laboratory has very kindly given me the records of all the Weil Felix reactions performed during 1931. There were twelve reactions performed, with human blood, during the year, two of which were positive (the two cases mentioned above).

Therefore in 1931 only 16.6% were positive.

I am assuming of course that these twelve cases were all suffering from the disease under discussion.

Was serum heated to 45°C?

Differential Diagnosis

From Typhoid Paratyphoid Fevers:

Temperature and moderately slow pulse with enlarged soft spleen may suggest Enteric.

The rash is seldom as profuse in typhoid but in those cases where the rash is sparse difficulty may arise though the intense headache, the constant feature of typhus, should put one right.

The bite and enlarged glands, if present, should save any confusion.

Diagnosis may be established by laboratory methods such as stool, blood culture and Widal reaction.

From Secondary Syphilis:

The rash of syphilis resembles very closely that of this disease, though in syphilis the rash is more indurated as a rule. Small shotty glands and sore throat may also lead to difficulty. In those cases with an initial bite the bite, especially if near the genitals as is frequently the case, may be confused with a syphilitic chancre (see photograph of ulcer).

Wasserman Reaction should always be positive in the secondary stage of syphilis and this should give one a positive diagnosis.

It may be as well to note two cases which have occurred in my series where diagnosis was in doubt.

Case 1. A young man was seen with a profuse papular rash over the whole body, including the palms of the hands and soles of the feet. The papules were palpable, rather sore and definitely indurated. The epitrochlear and other small glands were enlarged; they were not tender.

Temperature was 101° with a pulse rate under 100 per minute. Diagnosis rested between typhus and secondary syphilis. Although there had been no primary sore or any history of possible source of infection by the usual channels, a Wasserman reaction was performed and was reported as negative.

The temperature continued to vary between 98° and 100° daily for two months with other symptoms including swelling of the face, oedema of the turbinates, cough and sore throat. Headache, though present, was not severe.

The patient was sent down to South Africa for a change. Weil Felix reaction was negative at this time and the rash was still present, being a brown pigmentation resembling that seen in the convalescent typhus of Kenya. Owing to condylomata appearing another Wasserman was performed in South Africa, which was positive. Treatment was begun with 914 and the patient immediately started to recover. On his return to this country the patient looked fit and the rash had disappeared. The Wasserman was confirmed.

Case 2. A young married woman complained of slight headache and anorexia with a temperature up to 101° for two days; thereafter it only went up to 99°. On examination she had an angry-looking bite on the inner aspect of the thigh near the vulva and the glands in the groin were enlarged and tender.

On the fourth day a very scanty papular rash developed. Glands in the neck and epitrochlear glands were palpable, shotty but not tender. The throat was a little sore. I diagnosed a mild attack of Typhus; however, on consultation syphilis was suggested. I had by that time removed the bite under local anaesthesia for injection into a guinea-pig which incidentally showed no typical reaction. The patient was removed to the Infectious Diseases Hospital where she came under the care of the doctor in charge, who also diagnosed syphilis. A Wasserman reaction was performed which was negative. A provocative dose of 914 was administered and the Wasserman repeated a week later; this also proved negative. Weil Felix reaction was negative.

The patient was ill for about ten days in all.

Three months later a further Wasserman was performed but was again negative.

From Subtertian Malaria.

In the early stages this disease may be mistaken for malaria. Rigor, comparatively slow pulse and enlarged spleen may suggest malaria. The

small daily remission of the temperature may occur in an initial attack of subtertian malaria and this also may lead to confusion.

The presence of malarial parasites in the blood will confirm the diagnosis in the majority of cases, though the possibility of malaria complicating this disease should be borne in mind.

From Dengue Fever

Difficulty only arises when there is an epidemic of Dengue.

Joint pains, high fever and rash occur in Dengue, though the rash should not be mistaken and the remission period of Dengue is diagnostic.

From Measles

In the early stages of typhus, erythema and bloated expression with suffused eyes may suggest measles, but the absence of Koplick spots and the appearance of the true rash should prevent confusien.

Prognosis

The prognosis is good.

Jewell and Cormack in their paper give a mortality of 10%, i.e. two deaths in twenty-one cases. This is definitely too high an estimate in my opinion.

Anderson, who has practised in Kenya for over

Fig. 6.

SOURCE OF INFORMATION	NUMBER OF CASES.	RECOVERY.	DEATH.
GILKS	4	3	1
CLEARKIN	8	8	0
ANDERSON	5	5	0
DOIG	18	18	0
JEWELL & CORMACK	21	19	2
CASES IN EUROPEAN HOSPITAL in 1931 of which I know Result.	5	5	0
MY OWN CASES	29	29	0
HENDERSON	19	18	1
TOTAL CASES	109	105	4

MORTALITY 3·6 Per Cent.

ten years, has never seen a fatal case and he tells me he has an average of four or five cases a year. Doig of Nyeri has had no deaths in eighteen cases. Henderson reports one death in nineteen cases. Out of 109 cases of which I have been able to obtain records there have been 4 deaths, giving a mortality of 3.6% (fig.7).

Complications and Sequelae

Very few complications have been noted by previous writers. One case had a thrombosis of the internal saphena vein in both lower limbs and another a phlebitis of a vein in the left thigh and calf one month after the disease. This is of possible interest with regard to the pathology of the disease.

Broncho-pneumonia and pleurisy have been noted in two cases.

A mild jaundice has been noted as occuring during convalescence in one case.

Doig tells me that three of his cases were pregnant women and they all aborted.

In my series I have noted no complications and the sequelae have all been results of the severe toxaemia that occurs in this disease. The common result of this toxaemia is a myocarditis with, occasionally, an attack of tachycardia if

the patient gets up too soon or endeavours to do too much. This heart attack is alarming and worthy of note with regard to the convalescence. Generally there is no dilatation of the heart, but I have noted this in one case.

A continuance of the insomnia and nightmares for some weeks is a common sequela.

Further evidence of the results of the toxaemia on the nervous system was evident in one case where the patient who was a fairly heavy pipe smoker, developed a tobacco amblyopia after smoking three pipes in succession one evening soon after he had been allowed to get up.

General lassitude, inability to concentrate and anorexia remain for many months after a severe attack.

Treatment

Treatment is purely symptomatic, there being, as yet, no specific remedy.

The usual fever treatment should be given; fluids ad lib, soda-bicarbonate and glucose, careful attention to the bowels etc. For the headache I have found pyramidon to be the most useful drug. I give pyramidon gr.V, aspirin gr.V and caffeine citrate gr.II in a powder 4-hourly. Hot fomentations or ice packs to the head give some relief.

McRobert[7] in India suggests lumbar puncture to relieve the headache as he states that, in his cases, the fluid has been under pressure, but I have not found it necessary to give this method a trial.

For the insomnia I have found medinal to be as useful as any drug.

Arsenic in the form of stovarsol (gr.IV daily) seems to be beneficial though it does not shorten the course of the disease. The patient feels better for it and, I think, is less depressed.

Convalescence should be prolonged in view of the condition of the heart muscle and general debility.

My general rule has been to forbid the patient to return to work for at least a month, and that a fortnight of the month should be spent away from his usual environment. As all my cases have occurred at a height of over 5,000 ft. it would seem obvious that the patient should spend a fortnight of his convalescence at sea level if he wishes to recover quickly.

As an instance of this point, one of the most severe cases that I had came on a sea trip down to South Africa with me, at my suggestion, a week after the fever had subsided. Ten days later he was perfectly fit, the only evidence of his having had typhus being the residual staining of rash.

Patients undoubtedly take very much longer to recover if they remain at an altitude of 5,000 ft. or over and all should be strongly advised to go to a lower altitude for a short while.

Vector

The vector is unknown in Kenya. Lice I think can be excluded as the usual carrying agent in Kenya as the cases occur amongst the better classes, whose houses are kept clean and lice are seldom to be found. Ticks, mites, fleas and flies are all possibilities.

With regard to the ticks, these abound in the long grass and it would be difficult to find anybody who has not at some time or other found a tick biting him. Nearly every household keeps some domestic animal, such as a dog or a cat, who are continually bringing ticks and fleas into the house. Yet the disease has occurred in houses where no domestic animals are kept.

It is very difficult to get a history of a tick bite prior to the onset of fever, as tick bites are so very common. I have had evidence, as already described, of a fly, a tick and a minute animal - possibly a mite but more probably a tick - being the vector in three cases with an initial bite.

Henderson tells me he has evidence of a flea

and a tick causing the disease.

Doig also informs me that he has obtained a history of a tick bite prior to the onset of fever in 15 cases out of 18. All his cases have occurred on farms in the bush veldt, none in the two small townships that are in his province. He himself had the disease and he assures me that the only thing he was bitten by was the nymph of the tick Haemaphysatis Leachi, a dog tick. Only two of his cases had the typical initial lesion.

Zinsner and Castaneda[8] have proved that bed-bugs and lice are both capable of infecting a guinea-pig with Mexican typhus.

Mooser and Dumner[9] in the Southern States of America prove that Rickettsia from endemic typhus can live in the louse.

Shelmire and Dove[10] suggest that Liponyssus bacoli Hurst is the vector for the endemic typhus of Northern Texas.

Ticks are known to be the vectors for Rocky Mountain Fever and "Tick-bite Fever" of South Africa.

In California the Dermacentor Venestus is the tick responsible and in South Africa the Amblyomnia Hebreum, amongst others. Mites are known to be the vectors for the Tsutsugamushi Fever of Japan and Sumatra.

It becomes apparent that lice, ticks, mites and bed-bugs are all capable of conveying Typhus or typhus-like diseases elsewhere in the world, so it is possible that in Kenya there are two or more vectors.

Host

In my opinion time will show that the rodent is the animal host of the Rickettsia in Kenya and that the disease is conveyed to man from time to time by one or more of its fauna, such as the tick, mite or flea.

During the rainy season field rats are more abundant in houses, being driven from the grass and river banks by the wet weather; on the other hand, water rats spread farther afield at this time, receding to the rivers again during the dry weather.

It will have been noticed that it is at the two rainy seasons that the disease is more prevalent. In a letter to me, Doig wrote that all his cases occurred either during or shortly after the rainy season and that rats increased in numbers in the houses and stores at this season, being driven out of the bush by the heavy rains.

At present there are investigations proceeding at the Laboratory to endeavour to find out what part, if any, the rodent plays in the transmission

of the disease. Rats have been collected from the area in Nairobi where the disease is endemic and I understand that in a recent batch two rats were found to have a positive Weil Felix reaction, so I hope that those engaged on this work will have something concrete to publish at a later date.

As yet one is unable to explain the prevalence of the disease in August in connection with the migration of rodents.

Virus.

Animal inoculations have been performed in a few instances on my early cases, 5 cc. of the patient's blood being inoculated intraperitoneally into a guinea-pig, but the results have been negative or inconclusive.

It occurred to me that in those cases where there was an initial lesion, its removal and injection into a guinea-pig might give more satisfactory results. Accordingly I removed the bite from my next patient. This case, unfortunately, was seen first on the 8th day of the disease when the eschar was in the black scab stage, in fact when the virus, in all probability, was no longer active. The result of the injection was negative.

Soon after this I was called in to a case on the second day of the fever before the rash had appeared; in this case the initial lesion was in the early stage of small pustule with raised inflammatory area surrounding it. The pustule was situated on the thigh near the inguinal region and the glands draining this area were enlarged.

I removed the pustule together with the surrounding skin and subcutaneous tissue under local anaesthesia in such a way as to ensure the inclusion of the maximum amount of lymphatics possible in the area I removed. I then cut the piece of tissue in half in its long axis. One half was immersed in formol saline for section purposes and the other half was put into normal saline and given to Tonking of the Medical Research Laboratory who pounded it up with normal saline and injected 5 cc. of the emulsion intraperitoneally into two or three guinea-pigs. His findings will shortly be published in the Kenya Medical Journal. Suffice it to say that in eight days one of the pigs produced, in addition to fever, the typical enlargement and inflammation of the testes and adnexa as described by Mooser[11] in connection with Tarbidillo or Mexican Typhus.

The infection was kept up in a series of pigs by injection of blood from the positive pig.

Pigs were killed and microscopic and macroscopic examinations were made, Tonking using the technique advocated by Wolbach, Palfrey and Todd.[12] Rickettsia-like bodies were found in the brain and tunica vaginalis. Typical Typhus nodules were seen with the pervascular infiltration and endothelial reaction.

Tonking kindly let me examine some of his giemsa stained sections of brain and smears from the tunica. In the smears the small bodies were so numerous there could have been no mistaking them, and personally I could not differentiate them from the photographs of Rickettsia Prowazeki to be seen in Wolbach, Palfrey and Todd's book on Typhus.

Macroscopically the spleen was enlarged and it is interesting to note that the adrenal bodies were enlarged (Pijper[13] also mentions this with regard to pigs infected with Tick-bite Fever in South Africa). This may have some significance with regard to the lowering of the blood pressure which occurs in this disease.

Simultaneously with the removal of the eschar, 5 cc. of the patient's blood was injected

intraperitoneally into two guinea-pigs. The results were negative, the guinea-pigs having no rise of temperature or suggestion of illness.

Recently a further series of guinea-pigs were injected with an emulsion from the initial lesion of a new case and they developed the typical testicular reaction. So to date we have had two cases that have given positive results with the injection of the emulsion of the initial lesion in its early stage into a guinea-pig.

From the above experiments it would seem that in the early stages of the disease the virus remains local.

The mildness of the disease in Kenya may account for our failure to reproduce the disease in guinea-pigs by means of blood inoculation at the height of the fever. However, there are two methods which are open for investigation with more chance of successful results, namely splenic puncture and the preparation of the guinea-pigs by preliminary starvation, thereby causing them to be in a more receptive state to a mild infection. (Zissner and Castaneda[14] found that guinea-pigs and rats when fed on a vitamin deficiency diet get much more severe reactions to Typhus.

The Typhus Group of Fevers as they occur elsewhere in the world.

African Fevers

La Fievre Boutonnese as described by E. Conseil (15) in 1929 occurring in Tunis.

When reading E. Conseil's paper I had the immediate impression I was reading about Kenya Typhus.

Clinically the two diseases are identical. As in Kenya the tache noire with accompanying adenitis is by no means a constant feature, while the white blood count is within normal limits in the two diseases. Again in Fievre Boutonnese myocarditis is also the most constant sequela. Weil Felix reaction in both diseases is rarely positive.

The only difference I could find between Fievre Boutonnese and Kenya Typhus was the seasonal incidence. In Tunis the disease occurs at one period of the year, in the hot season, May to September, whereas in Kenya, where the climate is more constant, the disease occurs throughout the year, though there are marked seasonal rises in incidence.

Conseil in his paper produces a good case for the exact similarity between Fievre Boutonnese and the fevers occurring along the Mediterranean

coast in France and Italy, and variously named Fievre Exanthematique, erytheme infectieux, Marseilles Fever, febbre errutiva speciale. He contends that as they are identical diseases they should all be named Fievre Boutonnese.

G. Lemaire[16] describes a similar disease occurring in Algiers and suggests that the tick is the vector and states that the incubation period is short. All his ten cases had a tache noire.

West Africa

Davies and Johnson[17] in Nigeria and Corson[18] in the Gold Coast in 1921 described a disease resembling Dengue. The symptoms were similar to those of Kenya Typhus, headache, insomnia, joint and muscular pains and slow pulse being constant features. In Davies and Johnston's paper there was no mention of any initial lesion occurring amongst their cases. Corson described enlarged tender glands but there was evidently no bite or septic spot or it would have been mentioned.

There have been no more reports forthcoming from West Africa but from these early reports it seems that a similar or identical disease occurs in Nigeria and the Gold Coast.

South Africa

In 1911 there appeared reports from three different sources.

Sant'Anna[19] at Lorenco Marques reported cases of a mild fever occurring as the result of a tick bite, some cases only having malaise and enlarged painful glands and others with severe headache and high fever in addition. No mention was made of any rash.

Nuttall[20] reported some information he had received from Turner, Howard and Hindle of similar cases elsewhere, and he gave this disease the name "Tick-bite Fever." The ticks responsible among others were the larvae of Amblyomnia Hebreum found in the long grass where cattle had been grazing. All newcomers to the district were susceptible to the disease, the first attack conferring complete immunity.

In the same year McNaught[21] read a paper on Paratyphoid and described an outbreak near Pretoria of a disease which was labelled influenza or paratyphoid but which he considered was a clinical entity and resembled very closely a mild endemic Typhus as described by Brill in New York. His description was obviously one of a typhus-like disease. He also stated that Maher had seen very similar cases in another town which had been associated with the bite of a tick.

During the last two years Pijper has published five papers upon this subject, four in conjunction

with Helen Dau (13, 22, 23, 24) and one with Troupe (5).
He has made an extensive study of the disease, especially in the laboratory.

Pijper is of the opinion that there are two distinct diseases in South Africa, Typhus Exanthemus and what he has named "Tick-bite" fever after Nuttall. Pijper's work has been concentrated on so-called "Tick-bite" Fever and he tells us very little about Typhus as it occurs in South Africa. He remarks that "Tick-bite" Fever is a mild disease. It has no mortality, no sequelae, almost no complications." His description of the bite mark, which has been proved to be that of a tick, and the evidence of one's eyes from the photograph leave no doubt in one's mind that it is identical with the initial lesion seen in a certain percentage of Kenya cases. He describes two forms of the disease, a mild form with bite, local adenitis and slight fever, and a more frequent form with general symptoms, headache, rash etc.

In my own experience in Kenya I have seen one case which might correspond to Pijper's mild form. The patient had a bite, local adenitis, severe headache and fever lasting four days, but no rash; he remained at work and came to me because of the intense headache.

Doig writes with regard to cases at Nyeri (Kenya)

"All the young people here have at times been bitten by the small tick that causes severe local reaction with at times a sore very like a small malignant pustule, with no ill effects beyond local reaction."

Pijper's clinical description of the disease resembles closely that of Kenya Typhus.

He does not give any data with regard to the pulse rate, merely remarking that the pulse is fast, but not as fast as the temperature would lead one to suspect.

He differentiates between Tick-bite Fever and South African Typhus on clinical, pathological and serological grounds.

The clinical difference is presumably based solely on the presence or absence of the initial bite and accompanying adenitis.

The pathological difference is in the differential white cell count (see fig. 5). As we have already seen in Kenya, neither form of the disease has a constant type of count.

Serologically Pijper conclusively differentiates between Tick-Bite Fever and South African Typhus in man. He gives a table of seven cases of Tick-bite Fever; in four cases the Weil Felix reaction was positive to OX_{19} OX_2 and Kingsbury strains of B. Proteus and in three cases to Kingsbury alone, whereas in South African Typhus (three cases shown)

the reaction was positive to OX_{19} and OX_2 but not to Kingsbury. He suggests that possibly in Kenya with the use of all available strains of B. Proteus similar results will be forthcoming.

So far this has not been the case. Admittedly there has been no systematic investigation of the Weil Felix reaction in Kenya as yet, due partly to the fact that the majority of cases are treated by the private practitioner who has not the time, even if his patients would let him, to take several specimens of blood on different days during the convalescence, partly to the fact that there is only one Government Laboratory to serve the whole of Kenya.

Taking the results of 1931, we have seen that out of twelve cases in which the reaction was performed with OX_{19}, OX_2, Warsaw, Kingsbury and agglutinalibus, only two showed weak positive results on the 12th and 14th day respectively; of these two, one case would fall under Pijper's Tick-bite Fever group and the other under the Typhus group. Both cases reacted to the indol producing strains of B. Proteus, OX_{19}, and OX_2, and not to the Kingsbury.

	OX_{19}	OX_2	Warsaw	Kingsbury	Agg.
Cases with eschar 12th day	+ 1/80	+ 1/80	-	-	-
Cases without eschar 14th day	+ 1/250	+ 1/250	+ 1/250	-	-

This year one case has been positive to Kingsbury alone, but I have no information as to whether or not there was an initial bite present.

It is interesting to note that in one respect our results have coincided with Pijper's. He states that guinea-pigs infected with either Tick-bite Fever or South African Typhus show a positive reaction to Kingsbury and not to the other strains. He has a series of 45 guinea-pigs infected with Tick-bite Fever and 10 with Typhus, all of which reacted to Kingsbury alone. Anigstein(37) in the Malay States also noted that a rat infected from a case that was positive to OX_{19} showed a positive reaction to Kingsbury and not to the others.

A guinea-pig to which the disease was transmitted from my case with the eschar, whose Weil Felix reaction had been positive to OX_{19} and OX_2, showed a positive reaction to Kingsbury strain but was negative to OX_{19}. Similarly two rats that were caught in Kilimani area, as already mentioned, showed a positive reaction to Kingsbury strain.

With regard to animal inoculation and the virus, none of Pijper's guinea-pigs infected with Tick-bite Fever or South African Typhus, by means of an intra-peritoneal injection of patient's blood or the injection of a brain emulsion from an already infected guinea-pig, have shown the typical testicular reaction

that occurs in Tarbidillo or the two Kenya cases. Pijper's cases only showed the typical temperature charts and malaise as described by Wolbach, Palfrey and Todd working with European Typhus.

With regard to the virus and pathological findings in the guinea-pigs, Pijper's results coincide with those found in Kenya except with regard to the above-mentioned testicular reaction, typical typhus nodules being found in the brain and elsewhere and numerous small bodies indistinguishable from Rickettsia. He also mentions the enlargement of the adrenals.

So it appears that in South Africa there is a similar disease or diseases as in Kenya.

In Kenya no one who has had Typhus with an initial bite has yet developed Typhus without the initial lesion. It would be of interest to know whether a patient who has had Tick-bite Fever acquires an immunity to South African Typhus.

Apart from the presence or absence of a bite, the only difference between Tick-bite Fever and Typhus with any degree of certainty would appear to be the difference in the Weil Felix reaction, and then only in human beings.

It is impossible on Pijper's findings to differentiate between Tick-bite Fever and South African Typhus in the guinea-pig.

DIFFERENTIAL WHITE CELL COUNT

IN INDIA.

AUTHOR	CASE	POLYMORPHS	LYMPHOCYTES	L.MONONUCLEARS	EOSINOPHILS.
MEGAW	1.	62	26	12	0
SHETTLE AND ROY	2.	58	29	12	1
"	3.	60	26	14	0
"	4.	60	26	12	2
"	5.	59	27	14	0
"	6.	65	25	10	0
"	7.	70	21	9	0
GHOSE	1.	62	32	6	0

Fig. 7.

India

For some years various writers have reported cases of a fever resembling Typhus occurring in the highlands and central provinces of India. Megaw in conjunction with others and also on his own account has written numerous articles describing the disease clinically and etiologically as it occurs in India.

The clinical picture of the disease is similar to that of Kenya in many respects.

The rash has the same characteristics; it resembles a secondary syphilitic rash, having the same distribution and leaving a similar brown staining, but it has more tendency to become petechial.

Headache and joint pains are also the chief symptoms. Photophobia and conjunctival congestion are marked. The fever runs a similar course and the pulse rate is relatively slow, under 100 per minute.

The spleen is enlarged in a certain percentage of cases.

As regards the white blood count this is fairly normal but some observers state there is a slight leucocytosis.

The differential white cell count appears to be very similar to that found in Kenya with a tendency to an increase in the large-mono nuclears and absence of eosinophils (fig.VII).

The Seasonal incidence varies in India; in the highlands the disease occurs in summer and in the central provinces and plains in winter.

As in Kenya, observers in India have seldom been able to obtain a positive Weil-Felix Reaction.

In Megaw's earlier reports none were positive, but in a later report with Shettle and Roy two out of seven were positive 1 in 80 in the 19th day to B Proteus X 19.

Likewise, so far, they have had no success with animal inoculations by using a patient's blood injected intraperitoneally into a guinea pig.

In India none of those reporting cases i.e. Megaw[25], Rao[27], Shettle, Roy,[26] Ghose[28] and Basu mention the presence of any initial lesion with its accompanying adenitis. So in this respect they differ from 50% of the Kenya cases.

The vector is unknown in India but Megaw[25] is of the opinion that it is a tick. This opinion is based on the fact that the majority of the cases reported have occurred amongst the Army and better and cleaner living population and lice were not found. In Bhim Tal and Sal Tal where an outbreak occurred, no two cases occurred in the same house and Megaw is of the opinion it could not be a louse.

He himself had the disease some years before

and he believes that it was caused by the bite of a tick which he had "picked up" in the jungle in the same district and is of the opinion that the species was the Rhipicephalus Sanguinies.

On the other hand Crag[29] can see no reason why the louse should not have been the vector in the Bhim Tal cases. He states that, although the better class people had the disease, they were in close contact with porters and guides on fishing and shooting expeditions and that these men and the other inhabitants are infested with lice.

Supporting the theory that the louse is the carrying agent in India, Basu[30] reports that a number of children all living in the same house in Simla got the disease and numerous lice were found.

So as yet the vector has not been proved and there is a difference of opinion as to whether the louse or the tick is responsible.

In spite of the negative results with regard to the Weil-Felix Reaction and animal inoculation and finding of Rickettsia-like bodies, on clinical grounds alone the disease as described in India may be said to be very similar to its counterpart in Kenya.

Australia.

In 1927 Hone[31] described a disease resembling Typhus that he had been investigating for some years occurring in and around Adelaide.

The symptoms are similar to Kenya Typhus but there is no initial lesion. It is a mild disease, the mortality being 6%: of these all but one have been over the age of 60 years.

The spleen is sometimes enlarged and there is a leucopenia early on in the course of the disease which later becomes a slight leucocytosis. Headache and mental symptoms, insomnia and delirium are marked features. The seasonal incidence is summer and late autumn.

As yet apparently little or no work has been done in the investigation of the disease with regard to animal inoculation. The vector is unknown.

Hone is of the opinion that it is not the louse. He discusses the rodent factor in the transmission of the disease and is of the opinion that the rodent is the animal reservoir, as the majority of cases occur in certain definite areas (as in Nairobi) and also amongst workers in butcheries, food stores and other places where rats and mice are abundant.

He puts forward the theory that as there is no bite or apparent means of entry for the causal organism, the disease might possibly be acquired

by inhalation.

Since Hone's report Penfold and Corkhill (32) have described a case without any rash whatsoever in which the Weil-Felix Reaction was positive to Kingsbury and X 19 to a high titre of 1 in 300 This may have been one of those mild cases when the rash is very scarce and what signs there were present were overlooked.

Malay States, Sumatra & Dutch East Indies.

"Tropical" Typhus & Tsutsu Gamushi Fever.

The investigations of the Typhus-like Fevers that occur in these countries have progressed considerably further than in India or Australia.

Fletcher and Lesslar[33 & 34] have made an extensive study of the disease. Fletcher[35] in his early paper compares the disease in the F.M.S. to others. He states that the cases occurred amongst workers on land that had been allowed to lie fallow for some years. There was no ulcer in his cases and he discussed the possibility of rodents being a factor in the transmission of the disease. In later papers Fletcher and Lesslar are of the opinion that there are two types of fever in the F.M.S. and that thereis yet a third type first described by Schuffner identical with the Tsutsu Gamushi Fever that occursin Japan.

Schüffner's "Pseudo-Typhus" has the initial bite or ulcer and is conveyed to man by the bite of the Trombicula Akamushi and closely allied mites.

The two other types in Malay they name urban and scrub Typhus on account of their distribution.

The urban typhus occurs in the towns and shopkeepers are more liable to the disease than

those in business offices, which compares with Australia where it occurs in food stores.

The scrub typhus occurs on the estates away from towns.

The clinical features of the two types are similar to each other and to the types elsewhere in the world already discussed. It occurs in the hotter months and, as in Kenya, is a mild disease, the mortality being less than 5%. Lewthwaite[36] gives the mortality as 6.7%.

In the Malay States and Sumatra, Fletcher and his co-workers have had more success with the Weil-Felix Reaction than we have had in Kenya, and it is on the result of this reaction that they base their differentiation between the three types. The urban type reacts strongly to B.Proteus O.X.19 whereas the scrub reacts strongly to Kingsbury strain.

Tsutsu Gamushi also reacts to Kingsbury alone but only in very low titres.

This weak reaction and the presence of ulcer and accompanying adenitis serves to differentiate Tsutsu gamushi Fever from scrub typhus in the opinion of Fletcher and Lesslar.

Tsutsu gamushi Fever is rather more severe than the other types. The fever lasts about 20 days and nervous symptoms are more pronounced.

Fletcher and Lesslar had no success with animal inoculations using monkeys and guinea pigs.

Recently, however, Anigstein[37] made a preliminary report on the results of his experiments of animal inoculation from cases on the Palm Oil Estate near Kualalumpar where an outbreak of the disease occurred. He found that 11% of those inoculated had a febrile reaction 3 - 4 days after inoculation. In a few instances there was also Scrotal Swelling. On microscopic examination of smears and sections of brain he noted the presence of slender spiral shaped gram-negative bacilli and diplobacilli extra or intracellular and also minute coccal or bipolar coccobacilli in the mononuclear cells.

These were indistinguishable from Rickettsia. The brain sections showed perivascular infiltration and nodules of mononuclear and glia cells.

From this preliminary report it appears that similar results have been obtained as in Kenya and South Africa.

Anigstein states that guinea pigs showed only a slight virulence when inoculated with blood from patient but a similar reaction was noted.

It is interesting to note that typical scrotal swelling did occur in a few instances but not in every case as has so far happened in Kenya.

As already stated, when dealing with South Africa Anigstein noted a crossed agglutination with Warsaw and Kingsbury strains, the rat having the opposite reaction to the patient. So it is quite possible that he will find all rats react to the same strain of B. Proteus whether infected with Urban Typhus, Scrub Typhus or Tsutsu gamushi. If this is found to be the case it will tend to show that all three types are fundamentally the same disease.

Fletcher and Lesslar[34] make an interesting statement which suggests that Tsutsu gamushi possibly produces an immunity to Scrub typhus; they state that three Europeans had Tsutsu gamushi Fever but none of them developed scrub typhus which occurred soon after on the same estate. On the other hand Wolff[38] in the Dutch East Indies reports a case where a man developed Tsutsugamushi after having had Tropical Typhus. This is the only report I have been able to find in the literature where one person has had more than one type of the Typhus Fever group. Wolff also reported that a guinea pig, injected with blood from a "Tropical" Typhus patient developed a temperature and scrotal swelling on the 8th day.

The animal reservoir in these countries is

thought to be the rodent. It is known that the animal reservoir in Tsutsugamushi is the vole rat and Anigstein caught a rat on the Palm Oil Estate during the outbreak with typical symptoms, which suggests the possibility of a rat being the host in Scrub Typhus.

As regards the vector, it is known that the mite is the vector for Tsutsugamushi Fever, but the vector or vectors for Tropical Typhus (urban and scrub) are as yet unknown.

Japan.

Tsutsugamushi Fever has been known in Japan for many years where it is a disease that attacks those working on the banks of certain rivers at certain Seasons.

The symptoms are similar to the other types of fever already discussed, with headache, conjunctivitis and a typical rash developing on the 5th day. There is always an initial lesion and accompanying local adenitis. The Fever runs a rather longer course, lasting from 14-21 days.

The vector is the same mite that transmits Tsutsugamushi Fever of Sumatra. Recently Nagayo Tamiya, Mitamura and Sato (39) have published the finding of rickettsia-like bodies which they name Rickettsia Orientalis.

America.

Typhus-like Fevers have long been known in America. Brill first described the disease as it occurs in New York; this has since been proved to be a mild form of European Typhus Exanthemus. The disease is endemic in New York and is described in all the text books.

In the Western States of America another form of the disease was found and has been given the name Rocky Mountain Spotted Fever. It has been found that this disease is caused by the bite of ticks the Dermacentor Andersoni and venestus.

In Idaho the disease is mild, the mortality being about 5%, whereas in the adjoining State of Montana the mortality is as high as 90%. This is of interest as it shows that a disease can alter its virulence under slightly different conditions.

Endemic Typhus has been described in Northern Texas and South Carolina in the Southern States of America where it is said to be identical with Tarbidillo or Mexican Typhus which occurs across the border.

The clinical features of all the types of Typhus in America are very similar. Typical rash, headache and mental symptoms, fever with comparatively slow pulse, being features of all. They are all mild except Montana as already mentioned.

A considerable amount of work has been done in America, chiefly by workers in the Southern States, on animal inoculation and the Weil-Felix Reaction.

Mooser[11] states that Mexican Typhus, Rocky Mountain Spotted Fever and Endemic Typhus can be distinguished from Typhus Exanthemus and Brills Disease by the fact that all guinea pigs when inoculated intraperitoneally with Mexican Typhus always develop an enlargement of the testes and adnexa, whereas Typhus exanthemus and Brills Disease do not produce this enlargement of the testes. Rocky Mountain Spotted Fever and Endemic Typhus also generally produce a testicular enlargement in the guinea pig. Mooser was under the impression that the testicular reaction was peculiar to America, but as has already been shown it occurs in Kenya, Malay States and Dutch East Indies.

Pinkerton[40] also makes a similar statement with regard to the presence or absence of the testicular reaction, but confines his observations to Mexican typhus and Typhus Exanthemus.

Spencer and Maxcy[41] distinguished Rocky Mountain Fever from Mexican and Endemic Typhus by means of the Weil-Felix Reaction.

In Rocky Mountain Fever the reaction is positive to OX_{19} OX_2 and Kingsbury strains of

B. Proteus in the majority of cases late in convalescence, whereas in Endemic and Mexican Typhus it is only positive to OX_{19}.

Havens[42] states that in Brills disease the Weil-Felix is positive to OX_{19} in 95% of cases in dilutions of 1 in 80 upwards, so this would serve to distinguish Brills disease from Rocky Mountain Spotted Fever.

The vector is unknown in America, except in Rocky Mountain Fever, but lice and bed bugs amongst others are suspected, and, as already stated when dealing with the vector in Kenya, have been proved to be capable of conveying the disease experimentally.

Rickettsia have been demonstrated in the animals inoculated.

Mooser states that in Mexican typhus the rickettsia are found in enormous numbers in the tunica vaginalis; they are both extra and intra cellular and that there is an endothelial proliferation. Nodular lesions of the brain are not very well marked and he suggests this is on account of the mildness of the disease.

Mooser and Dumner[43] prove that the Rickettsia are the causal organisms of Mexican Typhus. They reproduced Mexican Typhus in a guinea pig in the usual manner and then injected

a monkey with the exudate from the tunica vaginalis of the guinea pig in which were a large number of Rickettsia. They then fed lice on the monkey and finally allowed the lice to infect another guinea pig which produced the typical testicular reaction with large numbers of Rickettsia in the exudate of the tunica. The Rickettsia passed from man → guinea pig → monkey → lice → guinea pig.

According to Zozaya[44] the organisms found in the exudate of the tunica are not infective for man. He reports an interesting experiment he performed. He injected a man with the exudate from the tunica of an infected guinea pig but there was no reaction. He then produced a typical attack of typhus in a man by injecting blood from a guinea pig that had been infected with Mexican Typhus.

He suggests that there are two organisms, one producing the scrotal reaction and the other in the blood. The organism in the blood is infective to man, whereas the other one is not infective. This requires further investigation before it can be considered the truth, as it has obvious fallacies.

If what Zozaya suggests is true, why should the monkey in Mooser and Dumner's experiment have become

infected with typhus?

Zissner and Castaneda[45] have been able to immunise guinea pigs against Mexican Typhus virus by peritoneal injections of formalised (0.2% formalin and normal saline) Rickettsia material from the tunica. They procured an active immunity with killed Kickettsia, thereby assisting to prove that Rickettsia are the causal organisms of Mexican Typhus and suggesting that the organism found in the tunica is the organism that produces typhus. If there had been two organisms the supposedly immunised guinea pigs should have produced (after the injection of blood from a typhus patient) a fever with typical nodules in the brain and other usual pathological findings but without the testicular reaction.. This was not found to be the case.

Europe.

Before dealing with Typhus Exanthemus, the fevers that occur along the Mediterranean coast and variously named Fievre Exanthematique, Eruptive Fever, Marseilles Fever, etc., must be mentioned.

As has already been seen these fevers, according to Conseil, are similar if not identical with Fievre Boutonnese. They are all mild fevers

with a seasonal incidence in summer and autumn.

Olmer and Olmer[46] reported only one death in their series of cases of Fievre Exanthematique and that was in a patient who was suffering from nephritis.

They state that nearly all the cases have a "tache noire" and that (as in Kenya) the "tache noire" with its accompanying adenitis is diagnostic. They suggest that the tache noire may be a chancre. This theory is interesting in view of the findings in Kenya where, as already suggested, the organisms are localised in the tache noire in the early stages.

Olmer[47] reports similar complications and sequelae as those seen in Kenya, namely, myocarditis and phlebitis, but he also reports two cases of intestinal haemorrhage, which appears to be unique.

With regard to the vector, all those who have reported cases seem to agree that the vector for these fevers is a tick. Vedrenne[48] reporting cases at Cannes suggests that the tick is the vector and connects the disease with the keeping of dogs.

Olmer and Olmer have proved to their own satisfaction that the tick responsible is a dog tick - the Rhipicephalus Sanguines. Durand[49] agrees with Olmer and Olmer. He collected 150 adult ticks of the R. Sanguines species from a

disused dog kennel and injected an emulsion of them into a guinea pig which developed typical fever three days later.

The Weil Felix Reaction is occasionally positive to B. Proteus X_{19} during convalescence. Burnet and Olmer[50] in 1927 were of the opinion that these fevers were the same as Brills disease and Tropical Typhus and they had negative results with animal inoculation. However, in 1930, Olmer states that Fievre Exanthematique, although the same as Fievre Boutonnese is different from Brills disease and Typhus Exanthemus. He inoculated a guinea pig with Fievre Exanthematique and then inoculated the same guinea pig at a later date with Typhus Exanthemus. The first inoculation did not immunise the guinea pig to Typhus, which it developed after the second inoculation. This interesting cross immunity experiment should be repeated before any definite conclusions can be made.

Typhus Exanthemus. Wolbach, Palfrey and Todd[12] have written an excellent book on the etiology and pathology of Typhus. Their clinical study of the disease took place at the St. Stanislaus Hospital in Warsaw. They had 181 cases through their hands and these were all selected on account

of their age, severity of fever and definite diagnosis. The mortality amongst these 181 cases was 13.26% but at the same time in the other Typhus Hospitals the general mortality was under 7%. Of the 181 cases 86 were men and 95 were women, most of them being from the lower classes in Warsaw and frequently 2 or more from the same family.

It would be as well to refer briefly to the symptoms and signs of the disease as described by the authors.

The onset was usually abrupt, patients having to give up work the same day as the fever began and there was malaise for a day or two prior to the true onset. Headache was present in 161 cases, being very severe, frontal and occipital, but diminishing or ceasing before the eruption developed.

Rigor - 134 cases.

Pain in back and limbs - 97 cases.

Vomiting - 53 cases.

Constipation - 157 cases; diarrhoea - rare.

Insomnia - 88 cases.

Conjunctival injection - 157 cases.

Flushed face - 73 cases.

Mental disturbance - 70 cases (45 excited, 25 dull).

Delirium was marked in 86 cases.

Signs of bronchitis or tracho-bronchitis in most cases.

Terminal broncho-pneumonia occurred in 18 cases.

Death occurred after the temperature had subsided in 11 cases.

The spleen was palpable in 48 cases.

The urine showed albumin in moderate amounts, but there was no signs of nephritis.

The blood pressure was abnormally low in all the 23 cases in which it was taken with a systolic under 80 m.m. and diastolic under 5 m.m. in several of them.

The average differential white cell count in 59 cases was Polymorphs 75.4%, Lymphocytes 18.6% and large mononuclears 5.9%. Eosinophils were absent in all counts.

The rash was small pink macules at the beginning with a distribution all over the body except the face. There was a rash on the face in only 6 cases and on the palms of the hands and soles of the feet in only 2 cases. The lesions became larger and more profuse and turned to a red colour gradually getting darker until they became purple. Some of the spots became palpable in 14 cases. The rash left no brown staining, the skin being quite clear when seen in the post mortem room in some cases where the temperature had subsided before

death took place.

The fever lasted for 10 - 14 days; the usual temperature chart was somewhat as follows. Temperature remained elevated the whole time at about 103° with small morning remissions and began to show a downward tendency during the second week. On the 11th or 12th day there was a marked drop almost to normal with distinct improvement in the patient's condition. This was followed by a two day rise and fall of temperature, after which the remperature remained normal. The pulse was rapid in comparison with the height of the temperature, but there was frequently a marked bradycardia after the temperature had subsided.

The complications and sequelae, apart from terminal broncho-pneumonia, were:-

Gangrene of skin in 6 cases.

Thrombosis of the iliac artery - 1 case.

Otitis media in 4 cases.

Deafness without middle ear disease in 5 cases.

Suppurative parotitis in 7 cases.

The Weil Felix was positive in all but 3.6% of the cases in which the reaction was performed. Agglutination took place as early as the 4th day of the disease, two strains of B. Proteus X_{19} being used.

The authors prove that Rickettsia Prowazeki

are the causal organisms of Typhus Exanthemus.

With regard to the pathology of the disease in man - the spleen was found to be enlarged but firmer than in Typhoid, the enlargement being present up to the end of the second week of the disease, after which the spleen became normal.

The liver showed a proliferation of the kupfer cells.

They describe the disease as one affecting the smaller blood vessels, there being a perivascular infiltration in the blood vessels of the skin and other tissues. The most typical findings were in the brain where the typical nodules of mononuclear and glia cells occurred together with the presence of large numbers of Rickettsia Prowazeki. The testes and adnexa showed a similar reaction around the smaller blood vessels as were to be found in the skin but were not comparable to the profuse reaction found in Rocky Mountain Spotted Fever.

In the guinea pig the brain showed the most typical reaction, but although they found nothing comparable with Rocky Mountain Spotted Fever and Endemic Typhus of the Southern States of America in regard to the swelling and profuse reaction of the testes and adnexa, they state that "the testes in the guinea pig are second only to the brain in

the number and typical character of the lesions."

The adrenal glands were occasionally engorged and showed a slight swelling.

SUMMARY

Clinical Manifestations of the Several Fevers.

It will have been noted that the symptoms and signs of all the fevers of this group are very similar.

The incubation period in the majority of fevers where it is known is about a week. The onset is sudden; headache, conjunctival congestion and pains in the back and limbs are marked features in the initial stages of all the fevers.

The rash appears on the 4th or 5th day and presents similar characteristics in all fevers of the group. There are two features of the rash that appear to be absent or are a rarity in Typhus Exanthemus (as described by Wolbach Palfrey and Todd) but which are present in all the other fevers; namely, the presence of the rash on the palms and soles and the residual staining of the rash.

The spleen is usually enlarged in the early stages of all the fevers.

Mental symptoms are present in them all, their severity appearing to vary with the amount of toxiemia present; the milder the fever the less the mental disturbance, but even in the mildest fever there is evidence of a mild delirium.

The temperature charts show a similar rise and fall in all the fevers and the majority end by rapid lysis.

The duration of the fever is from ten to fourteen days in all but Rocky Mountain Spotted Fever and Tsutsugamushi Fever which are both longer, being from fourteen to twenty-one days. The pulse rate tends to be relatively slow in all the fevers of this group except Typhus Exanthemus, in which it is rapid during the height of the fever but shows a very marked drop during convalescence.

The differential white cell counts show no constant deviation from the normal, except for the absence of eosinophils in the majority of fevers and the possible increase in large mononuclears in several of them.

In those fevers in which any investigation on the blood pressure has been carried out (Typhus Exanthemus, Kenya Typhus and Typhus of the East Indies), it has been found that the pressure is constantly low.

The mortality appears to be about 5% in the majority of the fevers, Tsutsugamushi, Rocky Mountain Spotted Fever of Montana and Typhus Exanthemus (in some epidemics) being the exceptions.

The commonest complication, as in almost every other fever, is broncho-pneumonia. A specific complication is gangrene and this has been noted in three of the group, namely Typhus Exanthemus, Brill's disease and Rocky Mountain Spotted Fever.

Initial Lesion.

It has been shown that the initial lesion, bite, eschar or tache noire occurs in Tsutsugamushi Fever of Sumatra, Malay States, Japan and East Indies, Mediterranean Fever, Kenya and South Africa. In all these countries except Japan it will be noted that by no means every case of a typhus-like fever has the initial bite with its accompanying adenitis.

Pijper in South Africa endeavours to prove that there are two distinct types of fever, namely South African Typhus and 'Tick-bite' Fever. Fletcher and Lesslar also submit that there are two types of fever in the Malay States and East Indies, namely Tropical Typhus and Tsutsugamushi Fever.

On the other hand, the investigators on the Mediterranean coast do not suggest that there are two types of fever but merely state the fact that some cases have a bite and others have no bite. Apart from the presence or absence of the bite with

adenitis, they cannot or do not attempt to differentiate between the cases on clinical grounds.

Vedrenne suggests that the bite occurs only when the vector leaves its head in the tissues, while Olmer and Olmer suggest that the bite may be a chancre. In Kenya I endeavoured to differentiate clinically by means of blood counts, temperature charts and symptoms etc. between those cases with an initial bite and those without, but I have been unable to do so.

Pijper bases his clinical differentiation on the differential white cell count and Fletcher and Lesslar on the severity of the fever and mental symptoms of Tsutsugamushi compared with Tropical Typhus. They both base their main differentiation on the Weil Felix Reaction, but clinically their differentiation is insufficient to refute the argument that on clinical grounds they may be said to be the same disease.

On reviewing the clinical manifestations of the fevers of this group, one is led to the conclusion that all the fevers of this group are fundamentally the same fever but vary in the degree of their severity.

Weil Felix Reaction

It has been agreed by all authorities that the Weil Felix Reaction is specific for Typhus Fever. Therefore it would appear that any fever giving a positive reaction over a dilution of 1/80, which has been suggested as the minimum dilution that indicates a definitely positive reaction, will belong to the Typhus group of fevers.

The reaction depends on the agglutination of the patient's serum with the Bacillus Proteus, This bacillus has been found in the urine and stool of typhus patients and was at first thought to be the causal organism, but this theory has since been rejected.

There have been a number of strains of B. Proteus isolated from time to time and they have been given the names X_2, X_{19} and Warsaw, These have been isolated in cases of European Typhus Exanthemus and are all indol-producing strains.

Some few years ago a further strain was isolated in the Malay States from a case of Tropical Typhus and was given the name Kingsbury after its discoverer, This strain is indol negative. A further strain has been isolated in South Africa and is known as Agglutinalibus.

Some fevers of this group react to the indol-

producing strains, others to the non indol-producing strains and yet again others to both. I have not been able to discover any that react to Agglutinalibus.

In the early investigations of some of the fevers of this group, the Weil Felix Reaction was found to be negative or rarely positive.

In 1923 Kelly[51] stated, with regard to Rocky Mountain Spotted Fever, that the reaction was negative in all nine cases on which he performed the reaction, and he concluded that the reaction was never positive in this fever. In 1930, however, Spencer and Maxcy stated that the reaction was positive in the majority of cases late in convalescence. Similarly, Megaw in his early reports states that the reaction is negative in Indian "Tick" Typhus, yet in a later report with Shettle and Roy two out of seven were positive. This has also been the case in Australia and on the Mediterranean coast.

In Kenya we have seen that some reactions are positive and, as has happened elsewhere, with increased knowledge in technique one will expect to find that more reactions are positive than was previously the case.

As suggested by Felix and Rhodes[52], it is possible that in those fevers in which the reaction

WEIL FELIX REACTION

INDOL+

(X_{19} X_2 Warsaw)

Typhus Exanthemus++
Brills disease++
Mexican Typhus++
Endemic Typhus of U.S.A. S. Africa.+
Kenya Typhus +−
Mediterranean Fevers+−
Indian 'Tick' Typhus+−
Tropical Typhus ++ (urban)

INDOL−

(KINGSBURY)

Tropical Typhus++ (Scrub)
Tsutsu gamushi Fever+

INDOL+ AND INDOL−

'Tick bite' Fever of S. Africa++

Rocky Mountain Spotted Fever++

Endemic Typhus of Australia (?)+

Fig.8.

is only weakly positive with any of the available strains, it may be found to be more strongly positive with a local strain. So far in Kenya no B. Proteus has been isolated from a case of Typhus. With the discovery of the Kingsbury strain many more fevers have given a strongly positive reaction, and it is very probable that there are further strains to be found in the countries where the disease occurs.

With regard to diagnosis, the Weil Felix Reaction is of little real value except in Typhus Exanthemus, as in most fevers the reaction only becomes positive late in the course of the disease and during convalescence.

In Typhus Exanthemus the reaction is positive as early as the fourth day and so it is of considerable value as an aid to diagnosis. Even in Typhus Exanthemus, however, the reaction is not always positive. In Wolbach, Palfrey and Todd's series 3.6% were negative.

The Weil Felix Reaction is the anchor on which some investigators hang their differentiation between the various types of the Typhus Fever group. In my opinion it is too early to classify the fevers of this group by means of this reaction.

In the accompanying table (Fig.VIII) it will be seen that the majority of the fevers fall under the

indol positive group and only four or possibly five (Australia) under the Kingsbury group, and of these five, three are also included in the indol positive group. The two remaining fevers that react to indol negative strain only, namely Scrub Tropical Typhus and Tsutsugamushi Fever, would therefore be classified in the same group.- yet Fletcher and Lesslar submit that they are different fevers. The group of fevers that react to both indol and non-indol strains includes Rocky Mountain Spotted Fever and "Tick-bite" Fever of South Africa. Both these fevers have a tick as their vector, yet "Tick-bite" fever has an initial lesion whereas Rocky Mountain Fever has no initial lesion. If one is consistent and classifies these two fevers under the same group, it would suggest that the presence or absence of an initial lesion is not sufficient evidence to differentiate one fever from another.

It will be seen that all the fevers of this group that have been discussed in this thesis, with the exception of West Africa (where little investigation has come to light) have shown a positive Weil Felix Reaction, which is further evidence to support the theory that all the fevers are fundamentally one and the same disease.

Virus and Animal Inoculation.

The virus of Typhus Exanthemus and Mexican Typhus has been proved to be Rickettsia. Rickettsia-like organisms have also been found in smears and sections of brain of guinea-pigs inoculated with Tropical Typhus, Tsutsugamushi Fever, "Tick-bite" Fever, Kenya Typhus, Brill's disease and Rocky Mountain Spotted Fever. They have yet to be found in India, the Mediterranean coast and Australia.

It is not the purpose of this thesis to discuss the question as to whether all these Rickettsia or Rickettsia-like organisms are the same organism. As yet there is insufficient evidence to enable one to come to any definite conclusion, but it is very suggestive that all these fevers are caused by the same organism and are therefore the same disease.

With regard to the testicular reaction in guinea-pigs found in America, Kenya and the Malay States, there is not sufficient evidence to give an opinion as to why this reaction should occur in these fevers and not in Typhus Exanthemus. There is evidence that there is a reaction of a mild degree in Typhus Exanthemus, but not sufficient to cause any swelling of the scrotum.

There is evidently some unknown factor to account for this and possibly Zoyaza's theory of there being two organisms is the correct one, but it is not possible to rely on his one experiment in order to come to any conclusion.

Vector and Reservoir.

It is known that there are a number of insects capable of transmitting the fevers of this group, but in only a few is it known which insect is the vector for the particular fever. The louse is known to be the vector for Typhus Exanthemus, the tick for "Tick-bite" Fever, Mediterranean Fevers and Rocky Mountain Spotted Fever, and the mite for Tsutsugamushi Fever.

Rickettsia (many of them non-pathogenic) have been found in lice, mites, bed-bugs, fleas and mosquitoes.

It would therefore seem possible for any insect to convey the disease to man. In Kenya, as has already been suggested, there may be two vectors, the tick being one of them.

Wolbach Palfrey and Todd state that 'all rickettsia have insect hosts which in the case of the pathogenic ones are the vectors.' This would indicate that the reservoir of these fevers is the vector and not one of the rodents. It has been suggested that the vole rat might be the reservoir in Tsutsugamushi Fever and there is strong presumptive evidence that rats play a part in the transmission of the disease in Australia, Kenya and the Malay States. In view of Wolbach, Palfrey and Todd's statement, it may be that the role

played by the rodent in these fevers is merely an indirect one, the rodent being the animal selected by the vector, e.g. the cat flea, mouse flea and fowl flea. Further evidence, as has already been suggested when dealing with Kenya, must be brought before a host other than the vector can be convicted of being responsible.

Classification.

In a group of fevers with so many different vectors there must obviously be certain variations in the form the disease takes and, in my opinion, it is because of the number of vectors and the consequent variations that occur that, as yet, these fevers have not been brought together into a group under one heading. It is generally recognised that these fevers all belong to the same group.

Megaw (53) suggests that these fevers should all be called Typhus but that they should be classified under their vector. He suggests

(Louse)	Typhus
(Tick)	Typhus
(Mite)	Typhus
(Unknown)	Typhus.

This seems to be as good a classification as is possible at the present stage of our knowledge of these fevers.

In conclusion, it is evident from the foregoing

that, in spite of slight differences in the Weil Felix Reaction and the presence or absence of an initial lesion, both of which must be considered in the future classification of these fevers, all the fevers in this group are fundamentally one disease, namely Typhus Fever. The only objection to this theory as far as one can see is the failure of Olmer's cross immunity experiment and the report by Wolff of a patient having had two of the fevers, namely Tropical Typhus and Tsutsugamushi. Neither of these reports has been confirmed yet, and until it has been proved beyond doubt to the contrary, the theory that all these fevere are variations of one disease, Typhus, is, in my opinion, the correct one.

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